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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/696,389	10/29/2003	Lawrence T. Boni	TRA-00801	6398

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EXAMINER	
KISHORE, GOLLAMUDI S	

ART UNIT	PAPER NUMBER
1612	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/696,389	BONI ET AL.	
	Examiner	Art Unit	
	Gollamudi S. Kishore, Ph.D	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 5-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 5-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The RCE dated 2-11-08 is acknowledged.

Claims included in the prosecution are 1 and 5--30.

In view of amendments, the 102 rejections over Deol, and Hersch have been withdrawn.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 1 and 5-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hersch (5,756,120) or WO 94/12155 in view of Gonda (US 2005/0019926) or vice versa.

Hersch as pointed out above teaches liposomal formulations containing amino glycosides for the treatment of the infections caused by Pseudomonas, M. avium and M. tuberculosis (col. 1, lines 38-62; col. 4, line 33 through col. 8, line 13, Examples and claims). What are lacking in Hersch are the claimed protocol of administration as claimed in instant claims and the pulmonary delivery of the composition... However, whether the composition has to be administered daily or once a day and the dosage

depend upon the severity of the condition, the age of the patient and other parameters, they are deemed to be obvious parameters manipulated by an artisan to obtain the best possible results. Hersch does not teach that the host infected with this organism has also cystic fibrosis. However, since the composition of Hersch is effective against this organism, it would have been obvious to one of ordinary skill in the art that the composition would be effective against this organism irrespective of whether the patient is suffering from other conditions.

WO teaches liposomal amino glycoside formulations containing phospholipids and sterol for the treatment of infections from micobacteria and pseudomonas. The lipid to drug ratios are between 9:1 to 3:1 (abstract, pages 1, 6-7 and examples). What are lacking in WO are the claimed protocol of administration as claimed in instant claims and the pulmonary delivery of the composition.

Gonda et al while disclosing liposomal formulations containing amino glycosides. According to Gonda et al, such formulations can be used for treatment of bacterial diseases in cystic fibrosis patients. The amino glycosides include tobramycin and amikacin. The composition is administered by pulmonary route (0011, 0027, 0060-0066, 0070 and 0089). Further according to Gonda, aerosol administration would result in targeted deposition of the composition in the desired parts of the respiratory tract (0074-0077). Gonda does not teach the lipid to drug ratios.

It would have been obvious to one of ordinary skill in the art to administer the composition of Hersch or WO by aerosol delivery (pulmonary) since Gonda teaches that using this route of administration for amino glycosides, one can achieve a targeted

deposition of the composition in the desired parts of the respiratory tract. Alternately, the use of appropriate lipid drug ratios in Gonda would have been obvious to one of ordinary skill in the art since as pointed out above, the amount of the drug depends upon several factors and the reference of Hersch shows the use of a wide range of lipid drug ratios.

Applicant's arguments have been fully considered, but are not persuasive. Applicant argues that Hersch at col. 5, lines 52-55 describes liposomes containing a neutral lipid, a phosphatidylglycerol, cholesterol and amikacin wherein the drug to total lipid ratios from 1:9 to 1:3 (lipid to drug ratio of 9:1 to 3:1) and that Hersch does not disclose a lipid to drug ratio of 1:2.5 or less as recited in the pending claims. This statement is incorrect since instant claims recite lipid to drug ratios of less than 2.5:1 (drug to lipid ratios of 1:2.5). The ratios of lipid to drug of 3:1 is closer to instant 2.5 :1 and applicant has not shown any criticality of the ratio claimed. Furthermore, as pointed out above, ratios are manipulatable parameters which depend upon the severity of the disease and patient's age and other factors. With regard to applicant's arguments that Hersch does not teach administered amount is 50 % or less, the examiner points out that the term, amino glycoside is a generic term and the amount of either the free drug or encapsulated drug depends upon the potency of the drug against a specific organism and applicant himself has not shown what the amounts of the free drugs are. Applicant's arguments that Hersch does not teach pulmonary administration of the composition are not persuasive since on

3. Claims 1 and 5-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gonda et al (US 2005/0019926).

Gonda et al while disclosing liposomal formulations containing amino glycosides. According to Gonda et al, such formulations can be used for treatment of bacterial diseases in cystic fibrosis patients. The amino glycosides include tobramycin and amikacin. The composition is administered by pulmonary route (0011, 0027, 0060-0066, 0070 and 0089). What is lacking in Gonda et al is the claimed protocol of administration as claimed in instant claims. However, whether the composition has to be administered daily or once a day and the dosage depend upon the severity of the condition, the age of the patient and other parameters, they are deemed to be obvious parameters manipulated by an artisan to obtain the best possible results.

Applicant's arguments have been fully considered, but are not persuasive. Applicant argues that Gonda lacks any teaching of suggestion with respect to the lipid/drug ratio and to administer the formulation according to the presently claimed method. These arguments are not persuasive since as pointed out above, the amount of the drug depends upon several factors and the protocol of administration depends upon the physician who is monitoring the disease. The examiner cites in this context, the reference of Popescu (4,981,692); see col. 8, lines 24-34. The term, amino glycosides includes several compounds which would vary in potency and applicants themselves have not shown that the same amount of drug is effective against several of the organisms claimed.

4. Claims 1 and 5-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lagace (5,662,929) in combination with Deol or vice versa.

Lagace teaches that chronic lung infection due to P. aeruginosa is a major cause of morbidity and mortality in patients with cystic fibrosis. According to Lagace P aeruginosa colonizes more than 90 % cystic fibrosis adolescents. Lagace teaches the encapsulation of amino glycosides in liposomes for the treatment of P. aeruginosa infections. One of the modes of administration taught by Lagace is aerosol (abstract, col. 3, line 7 through col. 6, line 16; col. 7, line 40 through col. 8, line 15; Examples). What is lacking in Lagace is the inclusion of cholesterol in the liposomes. What is also lacking in Lagace is the claimed protocol of administration as claimed in instant claims. However, whether the composition has to be administered daily or once a day and the dosage depend upon the severity of the condition, the age of the patient and other parameters, they are deemed to be obvious parameters manipulated by an artisan to obtain the best possible results.

The teachings of Deol have been discussed above. Deol further teaches that cholesterol-containing liposomes are more stable (page 169, col. 2 through 170, col. 1).

As pointed out above, the reference of Hersch shows the routine use of cholesterol in liposomes for the treatment of infections.

The use of cholesterol in the liposomes of Lagace would have been obvious to one of ordinary skill in the art since Deol teaches that cholesterol containing liposomes

are more stable. Alternately the use of amino glycosides in the liposomes of Deol would have been obvious to one of ordinary skill in the art since the liposomes taught by Deol successfully deliver the antibiotics at the site of the infection and therefore, one would encapsulate any antibiotic to treat a disease causing bacteria which is susceptible to that antibiotic.

Applicant's arguments have been fully considered, but are not persuasive. Applicant argues that Lagace teaches against the use of cholesterol and therefore, there is no motivation to use cholesterol. This argument would have been persuasive if the claims recite any specific percentages for sterol. Instant claims recite simply the presence of sterol which would even mean negligible amounts of cholesterol. If a minute amount of rigidity is in Lagace's liposomes is desired one of ordinary skill in the art would be motivated to use such small amount based on the teachings of Deol.

5. Claims 1-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lagace (5,662,929) in combination with Hersch (5,756,120).cited above.

Lagace teaches that chronic lung infection due to P. aeruginosa is a major cause of morbidity and mortality in patients with cystic fibrosis. According to Lagace P aeruginosa colonizes more than 90 % cystic fibrosis adolescents. Lagace teaches the encapsulation of amino glycosides in liposomes for the treatment of P. aeruginosa infections. One of the modes of administration taught by Lagace is aerosol (abstract, col. 3, line 7 through col. 6, line 16; col. 7, line 40 through col. 8, line 15; Examples). What is lacking in Lagace is the inclusion of cholesterol in the liposomes. What is also lacking in Lagace is the claimed protocol of administration as claimed in instant claims.

However, whether the composition has to be administered daily or once a day and the dosage depend upon the severity of the condition, the age of the patient and other parameters, they are deemed to be obvious parameters manipulated by an artisan to obtain the best possible results.

As pointed out above, the reference of Hersch shows the routine use of cholesterol in liposomes for the treatment of infections.

The use of cholesterol in the liposomes of Lagace would have been obvious to one of ordinary skill in the art with a reasonable expectation of success, since Hersch shows the routine use of cholesterol in liposomes for the treatment of infections.

Applicant's arugments have been fully considered, but are not persuasive. Applicant's arguments are similar to those put forward for the above rejection of claims over Lagace in combination with Deol and therefore, same response is deemed applicable.

Double Patenting

6. Claims 1 and 5-30 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 74-76, 78-84, 86-87, 94-95, 98-102 and 105-108 of copending Application No. 10/383,173 by itself or in combination with Lagace cited above. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims in both are drawn to a

method of treatment of diseases caused by the same organisms using the same liposomal compositions containing the same active agents. Instant claims recite the limitation that the patients having these organisms in addition suffer from cystic fibrosis. Since the active agents used are for the treatment of the infective disease itself and not the additional disease conditions the patient is suffering from, it would have been obvious to one of ordinary skill in the art to use the compositions irrespective of other disease conditions the patient is suffering from. One of ordinary skill in the art would be motivated to treat the same infective disease in cystic fibrosis patients since the reference of Lagace teaches that 90 % of cystic fibrosis patients are infected with P aeruginosa and that liposomal compositions containing the antibiotics could be used for the treatment.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

This rejection is maintained in view of applicant's request for holding the rejection in abeyance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S. Kishore, Ph.D whose telephone number is (571) 272-0598. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Krass Frederick can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Gollamudi S Kishore, Ph.D/
Primary Examiner, Art Unit 1612

GSK